UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/758,593	01/10/2001	Michael G. Walker	PC-0025 CIP	9627

27904 7590 05/20/2003

INCYTE CORPORATION (formerly known as Incyte Genomics, Inc.)
3160 PORTER DRIVE
PALO ALTO, CA 94304

EXAMINER
LI, RUIXIANG

ART UNIT	PAPER NUMBER
1646	20

DATE MAILED: 05/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/758,593	Applicant(s) WALKER, MICHAEL G.	
	Examiner Ruixiang Li	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

I. Status of Application, Amendments, and/or Claims

Claims 1 and 11 have been amended. Claims 1-12 are pending and under consideration.

The amendment filed in Paper No. 19 on April 2, 2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the four ankyrin domains are not supported by the original disclosure, they differ from originally disclosed domains (see bottom of page 10). The original ankyrin domains disclosed are: F151 to R183, L184 to K216, L217 to R249, and E250 to L282. The amended ankyrin domains are F149 to R181, L182 to K214, L215 to R247, and E248 to L280. The original ankyrin domains clearly differ from the amended ankyrin domains in their amino acid sequences. Since there is no support in the original disclosure for the amended ankyrin domains, applicants were not in possession of the amended ankyrin domains.

Applicant is required to cancel the new matter in the reply to this Office Action.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

II. Withdrawn Rejections

The rejection of claim 11 under 35 U.S.C.§ 112, 2nd paragraph as set forth at pages 4-5 of the previous office action (Paper No. 18, December 31, 2002) has been withdrawn in view of Applicants' amendment to the claim.

III. Claim Rejection under 35 USC § 101

(ii) 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

(ii) Claim 5 recites a host cell comprising a vector. Thus, the claim reads on a transgenic human, which is non-statutory subject matter. It is recommended that "a host cell" be replaced by "an isolated host cell" to overcome this rejection.

IV. Claim Rejections under 35 USC § 112, 1st paragraph (Enablement)

(i) The rejection of claim 10 under 35 U.S.C. §112, first paragraph, as set forth at pages 3-4 of the previous office action (Paper No. 18, December 31, 2002), remains.

Applicants argue that the term "differentiation expression" has been defined in the specification as "increased, upregulated, or decreased, down regulated" in a sample. Since the specification clearly describes the upregulation or increased expression of Ankrd2V in clear cell sarcoma of the skeletal muscle relative to normal muscle tissue, one skilled in the art would clearly interpret the use of the term "differentially expressed" as it is recited in the claim to refer only to the increased or upregulation of the gene in the diseased state (middle of page 6).

This has been fully considered but is not deemed to be persuasive for the following reasons, as well as for the reasons set forth at pages 3-4 of the previous office action (Paper No. 18, December 31, 2002). The claim recites the term "differentially expressed". The specification refers "differential expression" to "an increased, upregulated or present, or decreased, downregulated or absent, gene expression as detected by presence, absence, or at least two-fold changes in the amount of transcribed messenger RNA or translated protein in a sample" (page 7, lines 20-22)". The disclosure only enables a portion of the term "an increased, upregulated". While it is true that the proper interpretation of the term should be in light of the knowledge of one skilled in the art and the disclosure of the specification, the disclosure simply fails to enable an artisan to practice the invention commensurate in scope with the claim. One does not read selected limitations from the specification into the claims.

Applicants argue that the term "a standard" has a clear meaning in the art and the term would be interpreted in light of the knowledge of one skilled in the art and the disclosure of the specification (bottom of page 6). This has been fully considered but is not deemed to be persuasive for the following reasons, as well as for the reasons set forth at pages 3-4 of the previous office action (Paper No. 18, December 31, 2002). A standard indicates a specific numerical value that is obtained by comparing to "normal". Applicants only provide guidance on how one may determine it, but fail to disclose that particular value.

(ii) The following new grounds of rejections are set forth below:

Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, because the

specification does not reasonably provide enablement for one skilled in the art to use the invention commensurate in scope with the claims.

The factors that are considered when determining whether a disclosure satisfies enablement requirement include: (i) the quantity of experimentation necessary; (ii) the amount of direction or guidance presented; (iii) the existence of working examples; (iv) the nature of the invention; (v) the state of the prior art; (vi) the relative skill of those in the art; (vii) the predictability or unpredictability of the art; and (viii) the breadth of the claims. *Ex Parte Forman*, 230 USPQ 546 (Bd Pat. App. & Int. 1986); *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Claim 1 (part b) recites an isolated cDNA comprising a naturally occurring variant of the amino acid sequence of SEQ ID NO: 1 having at least 90% identity to SEQ ID NO: 1. Claim 1 (part c) recites an isolated cDNA comprising a biologically active fragment of SEQ ID NO: 1. Claim 2 (part b) recites a fragment of SEQ ID NO: 2 selected from SEQ ID NOS: 3-6. Claim 2 (part c) recites a variant of SEQ ID NO: 2 selected from SEQ ID NO: 7-10. Claims 3-12 depend from claim 1. Therefore, the claims encompass a genus comprising an enormous number of nucleic acids which vary greatly both in length and in nucleic acid composition. However, other than the cDNA comprising the nucleic acid sequence of SEQ ID NO: 2 that encodes SEQ ID NO: 1, the disclosure fails to provide sufficient guidance and information regarding the structural and functional requirements commensurate in scope with what is encompassed by the instant claims. The disclosure has not shown (i) which portions of SEQ ID NO: 2 are critical to the activity of the Ankrd2V of SEQ ID NO: 1; and (ii) what

modifications (e.g., substitutions, deletions or additions) one can make to SEQ ID NO: 2 will result in protein mutants with the same functions as the protein of SEQ ID NO: 2. The state of the art (See, e.g., Ngo, et al, *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz, et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495) is such that the relationship between sequence of a protein and its activity is not well understood and is not predictable. Excising out portions of a protein or modifications to a protein, e.g., by substitutions or deletions, would often result in deleterious effects to the overall activity and effectiveness of the protein.

It is further noted that claim 1 (part c) recites "a biologically active fragment". The term apparently encompasses all biological activities, for examples, from cell growth, differentiation, to immunological activities, since there is no unambiguous definition for the term in the instant disclosure. Clearly, the instant disclosure does not enable one skilled in the art to use a claimed fragment in term of all these activities because the molecule apparently has no direct role, e.g., in regulating immune responses. Claim 2 (part b) recites a fragment of SEQ ID NO: 2. However, sequence alignment shows that SEQ ID NO: 3 is not exactly a fragment of SEQ ID NO: 2 (See attached sequence alignment). Claim 2 (part c) recites a variant of SEQ ID NO: 2 selected from SEQ ID NO: 7-10. However, sequence analysis shows that SEQ ID NO: 7-10 only have 15.9%, 14.7%, 18.2%, and 13.6% match with SEQ ID NO: 2, which best local similarity 82.7%, 81.3%, 82.9%, and 85%, respectively (See attached sequence alignment). Thus, SEQ ID NO: 7-10 only shares some similarity with a small portion of SEQ ID NO: 2. The instant disclosure asserts that these cDNAs are particularly useful for producing

transgenic cell lines or organisms which model human disorders upon which potential therapeutic for such disorders may be tested (bottom of page 11 of specification). However, no specific disorders are disclosed. It would require undue experimentation for one skilled in the art to determine the specific disorder(s) that each variant is associated with because variants may have different biological functions. Therefore, one skilled in the art would not know how to use these variants.

In addition, claim 6 recites a method for using a cDNA to produce a protein, comprising culturing a host cell comprising a vector comprising the cDNA. However, it is well known in the art that only when the host cell comprising an expression vector comprising the cDNA is used, will a protein be produced. A cloning vector cannot be used for protein production. It is suggested that "A vector" be replaced by " An expression vector" in claim 4 to overcome this part of rejection.

Accordingly, the disclosure fails to enable such a myriad of the claimed nucleic acid molecules that not only vary substantially in length but also in nucleotide composition and fail to provide any guidance to those skilled generally on how to make and use the claimed genus of nucleic acid molecules. Thus, it would require undue experimentation for one skilled in the art to make and use the claimed genus of nucleic acid molecules embraced by the instant claims.

V. Claim Rejections under 35 USC § 112, 1st paragraph (New Matter)

Claims 1 and 3-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 (part b) recites a naturally occurring variant of the amino acid sequence of SEQ ID NO: 1 having at least 90% identity to the amino acid sequence of SEQ ID NO: 1. There is no support for in the instant disclosure (page 4, lines 22-23). Claim 1 (part c) recites a biologically active fragment of SEQ ID NO: 1 from about amino acid residue L182 to about amino acid residue K214 of SEQ ID NO: 1, whereas claim 1 (part d) recites an antigenic epitope of SEQ ID NO: 1 from about amino acid residue F136 to about amino acid residue L154 of SEQ ID NO: 1. The recited fragment and epitope are not supported by the original disclosure (see bottom of page 10).

VI. Claim Rejections under 35 USC § 112, 1st paragraph (Description)

The following new grounds of rejections are set forth below:

Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The description discloses a nucleic acid of SEQ ID NO: 2 that encodes an ankyrin repeat domain 2 protein variant (Ankrd2V)) of SEQ ID NO: 1. However, claim 1 is drawn to an isolated cDNA comprising a nucleic acid sequence encoding a naturally occurring variant of SEQ ID NO: 1 having at least 90% identity to the amino acid

sequence of SEQ ID NO: 1, or a biologically active fragment of SEQ ID NO: 1 from about amino acid residue F136 to about amino acid residue L154 of SEQ ID NO: 1. Claim 2 is drawn to an isolated cDNA comprising a fragment of SEQ ID NO: 2 selected from SEQ ID NO: 3-6 or a variant of SEQ ID NO:2 selected from SEQ ID NOS: 7-10. claims 3-12 depend from claim 1. The claims do not require that the nucleic acids possess any particular biological activity (claims 1 and 2), nor any particular conserved structure, or other disclosed distinguishing feature (claim 1, part b, and claim 2, part c). Thus, the claims are drawn to a genus of nucleic acids that is defined only by partial sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in claim 1 (part c) and claim 2 (part b) is a partial structure of SEQ ID NO: 1 or 2 and there is no functional limitation for the recited nucleic acids. The only factor present in claim 1 (part b) is recitation of having at least 90% sequence identity with SEQ ID NO: 1, and there is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of nucleic acids, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Therefore, only the isolated cDNA encoding Ankrd2V of SEQ ID NO: 1 (including SEQ ID NO: 2), but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

VII. Claim Rejection under 35 USC § 112, 2nd paragraph

(i) The rejection of claims 10 and 12 under 35 U.S.C.§ 112, 2nd paragraph as set forth at page 4 of the previous office action (Paper No. 18, December 31, 2002) remains.

Applicants argue that from the disclosure and the knowledge of one skill in the art, a "standard" would clearly be understood to encompass any source of normal musculoskeletal tissue and that comparison with such a standard would indicate the presence of clear cell sarcoma only on observing a higher degree of expression of the gene (bottom of page 7 of Applicant's response).

This has been fully considered but is not deemed to be persuasive because the instant disclosure fails to define unambiguously the term, "a standard", an artisan would not know the metes and bounds of the term. A standard indicates a specific numerical value that is obtained by comparing to "normal". Applicants only provide guidance on how one may determine it, but fail to disclose that particular value. Thus, use of the term " a standard" makes the claim indefinite.

Claim 12 is indefinite because it recites "peptide nucleic acids" and "regulatory molecules". Applicants argue that the terms are well known in the art and used accordingly throughout the specification. This has been fully considered but is not deemed to be persuasive because the term ""peptide nucleic acids" is not well known and the instant disclosure fails to define the term unambiguously. In addition, the specification only provides exemplary examples for the term "regulatory molecules". Since neither the art nor the specification provides an unambiguous definition for the term, the claim is indefinite.

(ii) Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because it recites the term "biologically active fragment". Since neither the art nor the instant disclosure defines the term unambiguously, one skilled in the art would not know the metes and bounds of the term because the term encompasses all biological activities, for examples, from cell growth, differentiation, to immunological activities. Claim 1 is indefinite also because it recites the term "the complement thereof". It is well known in the art that cDNA encodes an amino acid sequence whereas its complement does not encode the same amino acid sequence (even though it may encodes a number of short fragments). Claims 3-12 depend from claim 1.

Claim 2 is indefinite because SEQ ID NO: 3 is not a fragment as the claim recites (see attached sequence alignment).

VIII. Claim Objections—Minor Informalities

Claim 1 is objected to because it (part a) recites "an amino acid sequence of SEQ ID NO: 1". It appears that "The" (instead of "an") should be used. Appropriate correction is required.

IX. Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (703) 306-0282. The examiner can normally be reached on Monday-Friday, 8:30 am-5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 305-3014 or (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov]. All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Ruixiang Li
Examiner
May 9, 2003

Yvonne Eyler
YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600